79. The isolated antibody fragment of claim 75, wherein said antibody fragment is an antagonist of the polypeptide encoded by the human cDNA in ATCC Deposit No. 97853.

80. The isolated antibody fragment of claim 75, wherein said antibody fragment is an agonist of the polypeptide encoded by the human cDNA in ATCC Deposit No. 97853.

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81. A composition comprising the isolated antibody fragment of claim 75, and a carrier.

82. A method of producing the isolated antibody fragment of claim 75, comprising:

(a) introducing an immunogen into an animal; and

(b) recovering said antibody fragment.

83. A method of detecting the polypeptide encoded by the human cDNA in ATCC Deposit No. 97853 in a biological sample comprising:

(a) contacting a biological sample with the isolated antibody fragment of claim 75; and

(b) determining the presence or absence of said polypeptide in said biological sample.--

Remarks

Support for the Amendments

The specification has been amended to correct inadvertent errors and to comply with formalities. Support for the amendments to the specification is found throughout the specification as filed. More particularly, the specification has been amended to reposition and amend the

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reference to previous applications, to reflect the designation of Figures 1, 2, and 4 as Figures 1A and 1B, 2A and 2B, and 4A and 4B, to correct formalities in section headings, to reflect the new address of the American Type Culture Collection, to comply with 37 C.F.R. § 1.821(b), and to correct typographical and clerical errors. A substitute Sequence Listing is hereby submitted to correct a clerical error.

The heading: "Brief Description of the Figures" has been changed to "Brief Description of the Drawings."

All references to Figure 1 in the specification have been amended to recite Figure 1A and/or Figure 1B, as appropriate. Similarly, reference to Figure 2 has been changed to Figure 2A and 2B and reference to Figure 4 has been changed to Figure 4A and 4B.

Reference to sequence identifiers has been added to the brief description of Figures 1 and 2 on page 5 of the specification.

With respect to the correction of the NaCl and sodium citrate concentrations on page 11, lines 27-28 of the specification, Applicants submit that 5x SSC is a well-known solution used in hybridization solutions. SSC is normally made as a 20x stock solution, and then diluted accordingly for a particular use. The 20x SSC stock solution contains 3 M NaCl and 0.3 M trisodium citrate. *See, e.g., Gibco BRL Products and Reference Guide, 2000-2001* at page 22-24 (Exhibit A). To make a 5x SSC solution, the 20x solution must be diluted by one-fourth. Therefore, a 5x SSC solution contains 750 mM NaCl (3 M ÷ 4 = 750 mM) and 75 mM trisodium citrate (0.3 M ÷ 4 = 75 mM). One skilled in the art would have immediately recognized that the amount of ingredients listed in the specification for a 5x SSC solution was incorrect. Rather than describing a 5x SSC solution, made up of 750 mM NaCl and 75 mM trisodium citrate, the specification inaccurately listed the ingredient amounts for a 1x solution. The skilled artisan, in

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recognizing the typographical error, could have easily adjusted the amount of ingredients described in the specification to properly make a 5x SSC solution.

On page 11, line 29, Applicants have noted a typographical error in the amount of salmon sperm DNA. The inclusion of agents such as salmon sperm DNA as blocking agents is well known in the art. *See, e.g.,* Ausubel, *et al.*, *Current Protocols in Molecular Biology*, John Wiley & Sons, Inc., (1997) at page 2.10.7 (Exhibit B). One skilled in the art would know that salmon sperm DNA is present in hybridization solutions in µg/ml quantities and thus would immediately recognize the above-described typographical error in the specification. *See id.* Further, the skilled artisan, in recognizing the typographical error, could easily have adjusted the amount of ingredients described in the specification to properly included 20 µg/ml denatured, sheared salmon sperm DNA in the hybridization solution.

On page 11, line 30, a degree sign which was inadvertently omitted has been added.

On page 22, lines 3, 6, 21, and 24, Applicants noted a clerical error in the designation of a conserved cysteine residue. The paragraph beginning on page 21, line 34, and continuing to page 22, line 9, refers, *inter alia*, to "the mature form(s) of a secreted protein . . . ." *See* specification at page 21, line 35. Applicants inadvertently used the numbering of the mature amino acid sequence rather than that used in SEQ ID NO:2. Therefore, the conserved cysteine residue referred to in this paragraph is in position 109 of the *mature* amino acid sequence, but the actual position of the conserved cysteine residue in the *full-length* amino acid sequence (*i.e.*, SEQ ID NO:2) is at position 132. Reference to SEQ ID NO:2 will show that the amino acid residue at position 109 is alanine, not cysteine, and in fact, the first cysteine residue in the polypeptide is at position 132. Applicants submit that one of skill in the art would realize this clerical error and understand that the conserved cysteine residue indeed is at position 132. For example, on page

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22, lines 5-9, the reader is referred to Figure 2 to show that the cysteine residue is conserved among the four members of the TNF receptor family shown in the alignment. Figure 2A clearly indicates that the first cysteine which is conserved among all four sequences corresponds to residue 132 in DR4 (SEQ ID NO:2). *See* Figure 2A, lines 13-16 (SEQ ID NO:2 shown on line 16). The skilled artisan, in realizing that amino acid residue 109 is not cysteine, would immediately refer to Figure 2 for guidance as to the position of the conserved cysteine residue, and would realize that the conserved cysteine is actually residue 132.

Corrections of typographical errors on page 12, line 13, page 30, lines 4 and 37, and on page 39, line 29 are self-explanatory.

On page 33, line 7, there is a typographical error in the name of a herpes simplex virus gene. Support that the gene is actually designated "ICP34.5" is may be found in the attached abstract of Chou and Roizman, *J. Virol. 57*:629-637 (1986) (Exhibit C), the reference which originally identified ICP34.5 in herpes simplex virus.

On page 34, line 36, there is a typographical error in the name of the TNF-family ligand "lymphotoxin-α." Support that the ligand is actually designated "lymphotoxin-α," rather than lymphdtoxin, may be found in the attached abstract of Mauri, *et al.*, *Immunity* 8:21-30 (1998) (Exhibit D).

On page 37, line 34, there is a typographical error in the name of the bacterium *E. coli*. Applicants submit that it would be readily apparent to one of skill in the art what bacterial species was intended by Applicants.

Applicants assert that no new matter will be added to the specification if these formalities, clerical errors, and typographical errors are corrected, and respectfully request that the amendments to the specification be entered.

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Support for the added claims 22 to 83 may be found throughout the specification, for example, at p. 8, lines 26-27; p. 8, line 35; p. 9, lines 5-16; p. 10, lines 22-33; p. 11, lines 1-15; p. 20, lines 20-24; p. 27, lines 22-32, p. 28, lines 1-21; p. 28, lines 30-32; p. 29, lines 16-24; p. 32, line 35 to p. 33, line 2; p. 34, lines 10-21; p. 36, lines 12-16, and in Figure 3.

Support for the polypeptide fragments of claims 25 and 47 can be found, *e.g.*, in the specification at page 10, lines 15-19; page 21, line 34 to page 23, line 27; and in SEQ ID NO:1 at pages 48 and 49. Specifically, it is noted at page 22, lines 2-4 that polypeptides with N-terminal amino acid deletions up to the cysteine-132 residue (as amended) may retain some biological activity. The specification at page 22, lines 27-28, in discussing these polypeptides with N-terminal deletions, notes that "polynucleotides encoding these polypeptides also are provided." Similarly, it is noted at page 22, lines 34-35, that polypeptides with C-terminal deletions up to the cysteine-221 residue may retain some biological activity. The specification at page 23, lines 18-19, in discussing these polypeptides with C-terminal deletions, notes that "polynucleotides encoding these polypeptides also are provided." Finally, it is noted at page 23, lines 20-23, that a polypeptide of the present invention may have both the above-noted N-terminal and C-terminal deletions. Therefore, a person of ordinary skill would have understood the present inventors to have been in possession of the claimed subject matter.

Applicants assert that the foregoing claim amendments do not add new matter.

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The Sequence Listing

In compliance with 37 C.F.R. § 1.825(a), Applicants submit substitute sheets to amend the paper copy of the Sequence Listing as well as a substitute computer readable copy of the Sequence Listing. Applicants' Attorney hereby states that the changes made in the sequence listing do not include new matter.

In accordance with 37 C.F.R. § 1.825(b), the paper copy of the Sequence Listing and the computer readable copy of the Sequence Listing submitted herewith are the same.

Applicants have discovered that there was an inadvertent error in entering sequences into the Sequence Listing, which resulted in the mis-identification of the oligonucleotide sequences disclosed on pages 38 through 42. The oligonucleotide sequence on page 38, line 6, was inadvertently omitted from the sequence listing, therefore, the remaining three oligonucleotide sequences were misnumbered in the sequence listing. To correct this error, applicants submit herewith a substitute Sequence Listing, in which the oligonucleotide sequence disclosed on page 38, line 6, which was originally listed in the specification as SEQ ID NO:9 has been added as SEQ ID NO:12. Accordingly, the oligonucleotide sequence disclosed on page 41, lines 20-21 and on page 42, line 20, which was originally identified in the specification as SEQ ID NO:10, is actually SEQ ID NO:9, the oligonucleotide sequence disclosed on page 41, lines 22-23, which was originally identified in the specification as SEQ ID NO:11, is actually SEQ ID NO:10, and the oligonucleotide sequence disclosed on page 42, line 28, which was originally identified in the specification as SEQ ID NO:12, is actually SEQ ID NO:11. Appropriate amendments have been made to the specification to conform to the substitute sequence listing. Since all of these oligonucleotides were disclosed in their entireties in the specification, this amendment adds no new matter.

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Summary

It is respectfully believed that this application is now in condition for examination. Early notice to this effect is respectfully requested

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036.

Respectfully submitted,

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